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Amendments to the Claims:

Please cancel Claims 82 and 94 without prejudice or disclaimer; amend Claims 49, 56-62, 71, 73-80, 83-84, 86, 88-89, 98, 122 and 148; and add new Claims 151-154 as set forth below.

1-48. (Canceled)

49. (Currently amended) A substrate for a protein kinase, wherein the substrate is selected from the group consisting of:

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wherein F is phenylalanine, K is lysine, and R is arginine; and wherein the LINKER is selected from the group consisting of N-methyl glycine, L-proline, D-proline,

50-55. (Canceled)

56. (Currently amended) A substrate for a protein kinase <u>or a precursor of the substrate</u>, wherein the substrate <u>or the precursor</u> comprises:

a peptide substrate for the protein kinase, wherein the peptide comprises a serine, a threonine, or a tyrosine on a terminal end of the peptide;

at least one fluorophore, wherein a fluorophore is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide;

wherein the fluorophore is attached directly to the peptide or the fluorophore is attached to the peptide by a linker selected from the group consisting of

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wherein

- (i) the substrate is specific for a protein kinase subtype,
- (ii) the fluorophore is attached to the C-terminal end of the peptide,
- (iii) a fluorophore is attached to each terminal end of the peptide,
- (iv) a first fluorophore is attached to a terminal end of the peptide and a second fluorophore, with photophysical properties distinct from the first fluorophore, is attached to any nonterminal site on the peptide,

: and

- (v) the fluorophore is a 7-nitrobenz-2-oxa-1,3-diazole derivative, and/or
- (vi) the substrate further comprises a carbohydrate, a lipid or a nucleic acid.
- 57. (Currently amended) The <u>precursor of the</u> substrate of claim 148, wherein the photolabile side chain comprises the structure

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- 58. (Currently amended) The <u>precursor of the</u> substrate of claim 56, wherein the <u>precursor of the</u> substrate comprises a serine with a photolabile side chain that blocks phosphoryl transfer.
- 59. (Currently amended) The <u>precursor of a</u> substrate <u>for a protein kinase, where</u> the <u>precursor comprises SEO ID NO:3 and of elaim 56, wherein the substrate</u> has the structure

- 60. (Currently amended) The substrate or the precursor of the substrate of claim 148, wherein after removal of the photolabile side chain, phosphorylation by a protein kinase of the terminal serine, the terminal threonine, or the terminal tyrosine to which the fluorophore is attached produces at least a 20% change in fluorescence intensity.
- 61. (Currently amended) The substrate or the precursor of the substrate of claim 148, wherein after removal of the photolabile side chain, phosphorylation by a protein

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kinase of the terminal serine, the terminal threonine, or the terminal tyrosine to which the $\,$

fluorophore is attached produces at least a 20% increase in fluorescence intensity.

62. (Currently amended) The substrate or the precursor of the substrate of claim

148, wherein after removal of the photolabile side chain, phosphorylation by a protein

kinase of the terminal serine, the terminal threonine, or the terminal tyrosine to which the

fluorophore is attached produces at least a 20% decrease in fluorescence intensity.

63. (Previously presented) The substrate of claim 60, wherein phosphorylation of

the substrate by the protein kinase produces at least a 70% change in fluorescence

intensity.

64. (Original) The substrate of claim 63, wherein phosphorylation of the substrate

by the protein kinase produces at least a 100% change in fluorescence intensity.

65. (Original) The substrate of claim 64, wherein phosphorylation of the substrate

by the protein kinase produces at least a 150% change in fluorescence intensity.

66. (Original) The substrate of claim 65, wherein phosphorylation of the substrate

by the protein kinase produces at least a 250% change in fluorescence intensity.

67. (Previously presented) The substrate of claim 56, wherein the substrate is

specific for a protein kinase subtype.

68. (Original) The substrate of claim 67, wherein the substrate is specific for

protein kinase C.

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69. (Original) The substrate of claim 68, wherein the substrate is specific for

isoforms α , β , and γ of protein kinase C.

70. (Withdrawn) The substrate of claim 67, wherein the substrate is specific for

protein kinase A, protein kinase B, protein kinase D, protein kinase G, Ca+/calmodulin-

dependent protein kinase, mitogen-activated protein kinase, protein kinase mos, protein

kinase raf, protein tyrosine kinase, tyrosine kinase abl, tyrosine kinase src, tyrosine kinase ves, tyrosine kinase fps, tyrosine kinase met, cyclin-dependent protein kinase, or cdc2

kinase

71. (Currently amended) The substrate or the precursor of the substrate of claim

56, wherein the substrate further comprises a carbohydrate, a lipid or a nucleic acid.

72. (Canceled)

73. (Currently amended) The substrate or the precursor of the substrate of claim

56, wherein the fluorophore is attached to the C-terminal end of the peptide.

74. (Currently amended) The substrate or the precursor of the substrate of claim

56, wherein the fluorophore is attached to the N-terminal end of the peptide.

75. (Currently amended) The substrate or the precursor of the substrate of claim

56, wherein a fluorophore is attached to each terminal end of the peptide.

76. (Currently amended) The substrate or the precursor of the substrate of claim

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75, wherein fluorophores with distinct photophysical properties are attached to different

terminal ends of the peptide.

77. (Currently amended) The substrate or the precursor of the substrate of claim

56, wherein a first fluorophore is attached to a terminal end of the peptide and a second

fluorophore, with photophysical properties distinct from the first fluorophore, is attached

to any nonterminal site on the peptide.

78. (Currently amended) The substrate or the precursor of the substrate of claim

56, wherein the fluorophore is a 7-nitrobenz-2-oxa-1,3-diazole derivative.

79. (Withdrawn and Currently amended) The substrate or the precursor of the

substrate of claim 56, wherein the fluorophore comprises a fluorescein group.

80. (Withdrawn and Currently amended) The substrate or the precursor of the

substrate of claim 56, wherein the fluorophore comprises a dansyl group, an acridine

group, an Alexa Fluor® group, a BODIPY® group, an Oregon Green® group, a

Rhodamine Green group, a Rhodamine Red-X group, a Texas Red® group, a Cascade

Blue $\underline{\hbox{\it l\hskip -2pt R}}$ group, a Cascade Yellow group, a Marina Blue $\underline{\hbox{\it l\hskip -2pt R}}$ group, a Pacific Blue group, an

AMCA-X group, or a coumarin group.

81-82. (Canceled)

83. (Currently amended) A precursor for a substrate for a protein kinase, wherein

the <u>precursor for the</u> substrate comprises:

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a peptide comprising a serine, a threonine, or a tyrosine on a terminal end of the peptide;

at least one fluorophore, wherein a fluorophore is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide; and

a photolabile side chain attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide, wherein the photolabile side chain blocks transfer of a phosphoryl group from adenosine triphosphate to a hydroxyl moiety of the serine, the threonine, or the tyrosine so that the substrate cannot be phosphorylated by a protein kinase until the photolabile side chain is removed from the substrate, and

wherein the the photolabile side chain comprises the structure

anc

wherein the fluorophore is attached to the peptide by a linker selected from the group consisting of a carboxamide linker, an aminobenzoic acid linker, a sulfonamide linker, a urea linker, a thiourea linker, an ester linker, a thioester linker, an alkylamine linker, an arylamine linker, an ether linker, and a thioether linker.

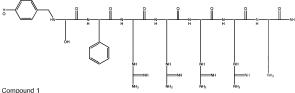
84. (Withdrawn and Currently amended) The substrate or the precursor for the <u>substrate</u> of claim 56, wherein the fluorophore is attached to the peptide by a linker selected from the group consisting of N-methyl glycine, L-proline, D-proline,

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85. (Canceled)

- 86. (Currently amended) A composition comprising the substrate or the precursor for the substrate of claim 56, and a carrier.
- (Original) The composition of claim 86, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.
- 88. (Currently amended) A chemical compound comprising SEQ ID NO:3 selected from the group of compounds consisting of:

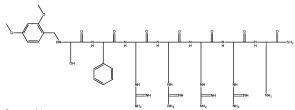


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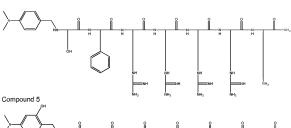
Compound 2

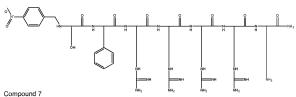
Compound 3



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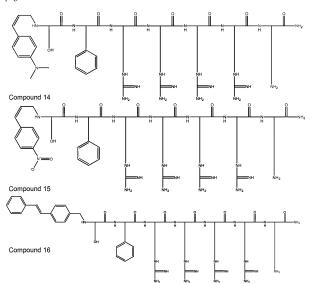


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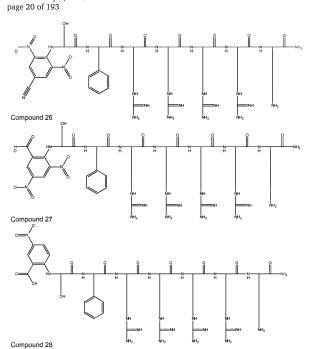
Compound 20

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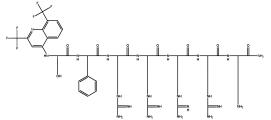
Compound 23

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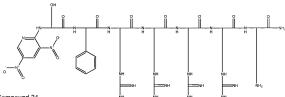


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Compound 29



Compound 30



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Compound 35

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Compound 38

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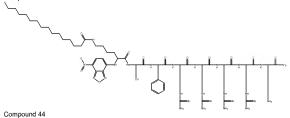
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Compound 40

Compound 41

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Compound 45

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Compound 46

Compound 47

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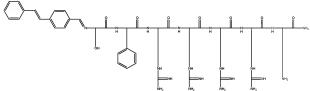
Compound 49

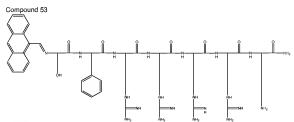
Compound 50

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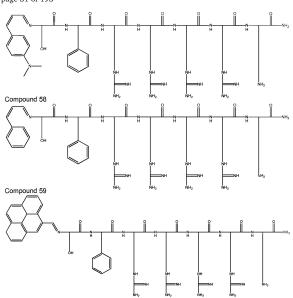
Compound 52





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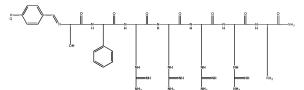
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Compound 61

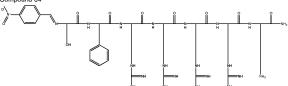
Compound 62

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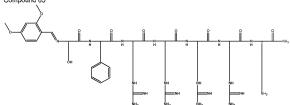
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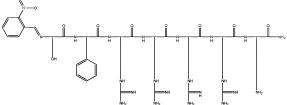
Compound 64



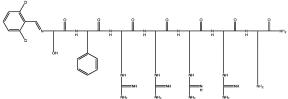
Compound 65



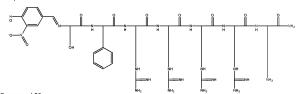
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Compound 67



Compound 68



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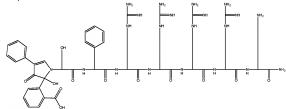
Compound 71

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Compound 77

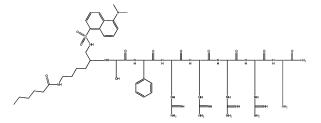


Compound 78

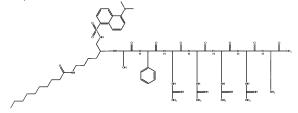
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Compound 80

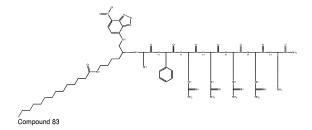
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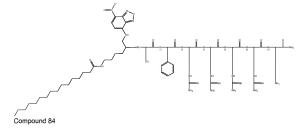


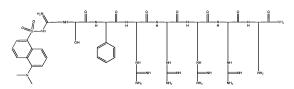
Compound 81



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Compound 85

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Compound 86

Compound 87

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Compound 89

Compound 90

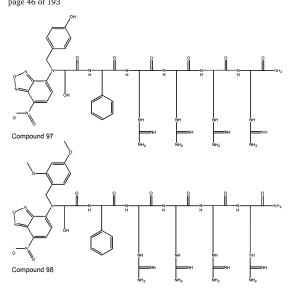
Compound 91

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Compound 156

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Compound 203

Compound 204

Compound 205

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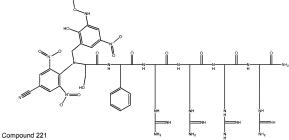
Compound 213

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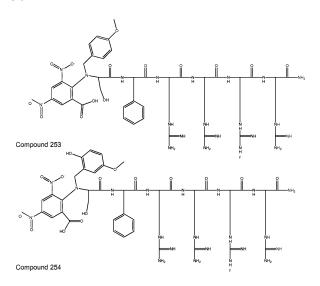
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Compound 249

Compound 250

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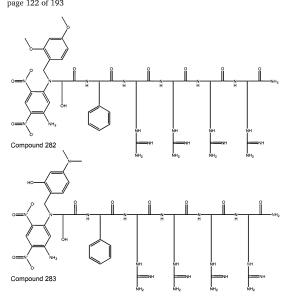
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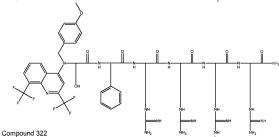
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Compound 315

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Compound 323 Compound 324 Compound 325

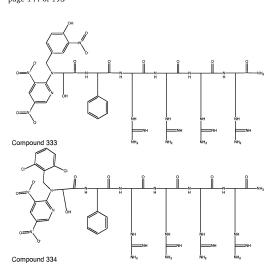
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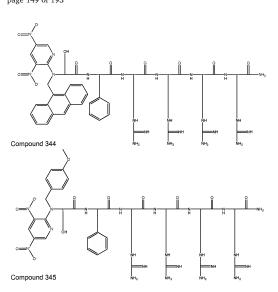
Compound 335 Compound 336

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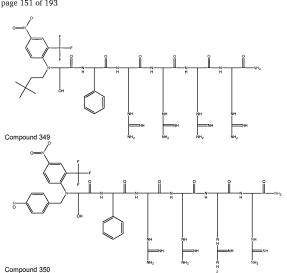


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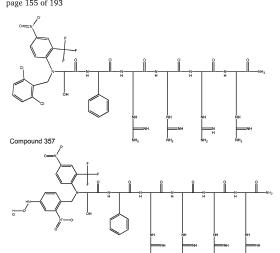


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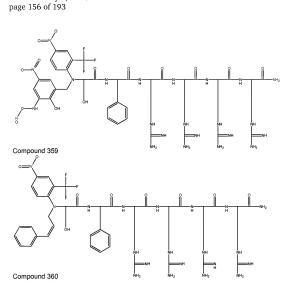
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Compound 358

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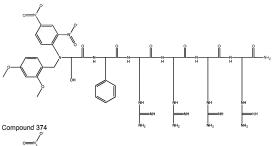
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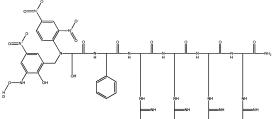


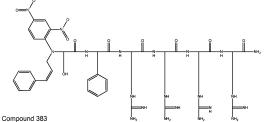
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Compound 384

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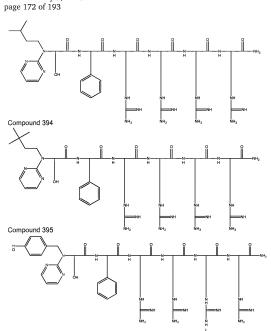
Compound 386

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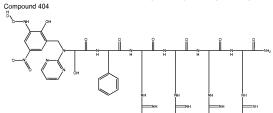
Filed: January 9, 2004



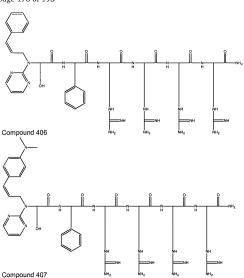
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Compound 411

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Compound 415

wherein amino acid chains are indicated as follows:

- -OH represents serine,
- -NH2 represents lysine,

represents phenylalanine.

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89. (Currently amended) A chemical compound $\underline{\text{comprising SEO ID NO:1}}$ having the structure:

wherein the LINKER is selected from the group consisting of the following:

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90. (Previously presented) A chemical compound having the structure: fluorophore-LINKER-X-FRRRRK-amide (SEQ ID NO:3);

wherein F is phenylalanine; K is lysine; R is arginine; and X is serine, threonine, or tyrosine, and wherein the linker is selected from the group consisting of a carboxamide linker, an aminobenzoic acid linker, a sulfonamide linker, a urea linker, a thiourea linker, an ester linker, a thioester linker, an alkylamine linker, an arylamine linker, an ether linker, and a thioether linker.

- (Original) The chemical compound of claim 90, wherein the fluorophore is a 7-nitrobenz-2-oxa-1,3-diazole derivative.
- 92. (Previously presented) The chemical compound of claim 90, wherein the fluorophore comprises a fluorescein group.

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93. (Currently amended) The chemical compound of claim 90, wherein the fluorophore comprises a dansyl group, an acridine group, an Alexa Fluor® group, a BODIPY® group, an Oregon Green® group, a Rhodamine Green group, a Rhodamine Red-X group, a Texas Red® group, a Cascade Blue® group, a Cascade Yellow group, a Marina Blue® group, a Pacific Blue group, an AMCA-X group, or a coumarin group.

94-95. (Canceled)

96. (Previously presented) A chemical compound having the structure: fluorophore-LINKER-X-FRRRRK-amide (SEQ ID NO:3);

wherein F is phenylalanine; K is lysine; R is arginine; and X is serine, threonine, or tyrosine, wherein the linker is selected from the group consisting of N-methyl glycine, Lproline, D-proline,

fluorophore-LINKER-X-FRRRRK-amide (SEQ ID NO:3);

wherein F is phenylalanine; K is lysine; R is arginine; and X is serine, threonine, or tyrosine, wherein the linker is selected from the group consisting of the following:

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- 98. (Currently amended) The chemical compound of claim 90, wherein the chemical compound is a substrate for a protein kinase or a precursor for a substrate for a protein kinase.
- (Original) The chemical compound of claim 98, wherein the chemical compound is specific for protein kinase C.
- 100. (Original) The chemical compound of claim 99, wherein the chemical compound is specific for isoforms α , β , and γ of protein kinase C.
 - 101. (Original) The chemical compound of claim 98, the chemical compound is

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specific for protein kinase A, protein kinase B, protein kinase D, protein kinase G, Ca*/calmodulin-dependent protein kinase, mitogen-activated protein kinase, protein kinase mos, protein kinase raf, protein tyrosine kinase, tyrosine kinase abl, tyrosine kinase src, tyrosine kinase yes, tyrosine kinase fps, tyrosine kinase met, cyclin-dependent protein kinase, or cdc2 kinase.

102. (Original) The chemical compound of claim 90, wherein the chemical compound further comprises a carbohydrate, a lipid or a nucleic acid.

122. (Currently amended) A chemical compound <u>comprising SEQ ID NO:3</u> having the structure

123. (Previously presented) A composition comprising a chemical compound of claim 89, and a carrier.

124-126. (Canceled)

127. (Previously presented) The substrate of claim 60, wherein the substrate

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comprises a metal ion chelator.

128. (Original) The substrate of claim 127, wherein the metal ion is a magnesium

ion or a calcium ion.

129. (Previously presented) The chemical compound of claim 90, wherein a metal

ion chelator induces a change in fluorescence intensity.

130. (Original) The chemical compound of claim 129, wherein the metal ion is a

magnesium ion or a calcium ion.

131. (Original) The chemical compound of claim 129, wherein the change in

fluorescence intensity is at least a 20% change in fluorescence intensity.

132. (Canceled)

133. (Previously presented) The chemical compound of claim 90, wherein the

linker comprises a turn to position the fluorophore in a location closer to the serine, the

threonine or the tyrosine than the location the fluorophore would occupy in the absence $\frac{1}{2}$

of a turn in the linker.

134. (Previously presented) The chemical compound of claim 89, wherein the

linker comprises a turn to position the fluorophore in a location closer to the terminal

serine, the terminal threonine or the terminal tyrosine than the location the fluorophore would occupy in the absence of a turn in the linker.

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135-136. (Canceled)

137. (Previously presented) The composition of claim 123, wherein the

composition is a pharmaceutical composition and the carrier is a pharmaceutically

acceptable carrier.

138. (Previously presented) A composition comprising the substrate of claim 49,

and a carrier.

139. (Previously presented) The composition of claim 138, wherein the

composition is a pharmaceutical composition and the carrier is a pharmaceutically

acceptable carrier.

140. (Previously presented) A composition comprising the compound of claim 88,

and a carrier.

141. (Previously presented) The composition of claim 140, wherein the

composition is a pharmaceutical composition and the carrier is a pharmaceutically

acceptable carrier.

142. (Previously presented) A composition comprising the compound of claim 90,

and a carrier.

143. (Previously presented) The composition of claim 142, wherein the

composition is a pharmaceutical composition and the carrier is a pharmaceutically

acceptable carrier.

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144-145. (Canceled)

146. (Previously presented) A composition comprising the compound of claim 122, and a carrier.

147. (Previously presented) The composition of claim 146, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

148. (Currently amended) The substrate of claim 56.

A substrate for a protein kinase or a precursor of the substrate, wherein the substrate or the precursor comprises:

a peptide substrate for the protein kinase, wherein the peptide comprises a serine, a threonine, or a tyrosine on a terminal end of the peptide;

at least one fluorophore, wherein a fluorophore is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide;

wherein the fluorophore is attached directly to the peptide or the fluorophore is attached to the peptide by a linker selected from the group consisting of

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wherein a photolabile side chain is attached to the serine, the threonine, or the tyrosine on the terminal end of the peptide, wherein the photolabile side chain blocks transfer of a phosphoryl group from adenosine triphosphate to a hydroxyl moiety of the serine, the threonine, or the tyrosine so that the substrate cannot be phosphorylated by a protein kinase until the photolabile side chain is removed from the substrate.

 149. (Previously presented) A composition comprising the substrate of claim 83, and a carrier.

150. (Previously presented) The composition of claim 149, wherein the composition is a pharmaceutical composition and the carrier is a pharmaceutically

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acceptable carrier.

151. (New) A composition comprising the precursor of a substrate for a protein kinase of claim 59, and a carrier.

152. (New) The composition of claim 151, wherein the composition is a

 $pharm acceutical \ composition \ and \ the \ carrier \ is \ a \ pharm acceutically \ acceptable \ carrier.$

153. (New) A composition comprising the substrate for a protein kinase or a

precursor of the substrate of claim 148, and a carrier.

154. (New) The composition of claim 153, wherein the composition is a

pharmaceutical composition and the carrier is a pharmaceutically acceptable carrier.

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